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Disease burden of urinary tract infections among type 2 diabetes mellitus patients in the U.S.

Shengsheng Yu [a,*], Alex Z. Fu [b], Ying Qiu [a], Samuel S. Engel [a], Ravi Shankar [a], Kimberly G. Brodovicz [a], Swapnil Rajpathak [a], Larry Radican [a]

[a] Merck Sharp & Dohme Co., 1 Merck Drive, P.O. Box 100, Whitehouse Station, NJ 08889
[b] Georgetown University Medical Center, 3300 Whitehaven Street NW, Suite 4100 - Milton Harris Bldg. Washington, DC 20007

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ABSTRACT

Aims: Type 2 diabetes is a reported risk factor for more frequent and severe urinary tract infections (UTI). We sought to quantify the annual healthcare cost burden of UTI in type 2 diabetic patients.
Methods: Adult patients diagnosed with type 2 diabetes were identified in MarketScan administrative claims data. UTI occurrence and costs were assessed during a 1-year period. We examined UTI-related visit and antibiotic costs among patients diagnosed with UTI, comparing those with versus without a history of UTI in the previous year (prevalent vs. incident UTI cases). We estimated the total incremental cost of UTI by comparing all-cause healthcare costs in patients with versus without UTI, using propensity score-matched samples.
Results: Within the year, 8.2% (6,014/73,151) of subjects had ≥1 UTI, of whom 33.8% had a history of UTI. UTI-related costs among prevalent versus incident cases were, respectively, $603 versus $447 ($p = 0.033$) for outpatient services, $1,607 versus $1,819 ($p$ = NS) for hospitalizations, and $61 versus $35 ($p < 0.0001$) for antibiotics. UTI was associated with a total all-cause incremental cost of $7,045 (95% CI: 4,130, 13,051) per patient with UTI per year.
Conclusions: UTI is common and may impose a substantial direct medical cost burden among patients with type 2 diabetes.

1. Introduction

Type 2 diabetes is a chronic, progressive metabolic disorder resulting from the loss of early insulin secretion and development of insulin resistance (De Fronzo, 1999). In the United States, the incidence of diabetes nearly tripled between 1990 and 2010, with 1.9 million new cases diagnosed in 2010 (Centers for Disease Control, 2013). Patients with type 2 diabetes are at an elevated risk of a number of other medical conditions compared to non-diabetic individuals, including cardiovascular disease, eye problems and blindness, renal disease, and lower extremity amputations. Type 2 diabetes is also considered an immunocompromised state and is a known risk factor for certain infectious diseases (Muller et al., 2005; Shah & Hux, 2003).

Urinary tract infections (UTIs) are the most common type of bacterial infections (Foxman, 2002). Asymptomatic bacteriuria and symptomatic UTI are both reported to be more frequent in patients with type 2 diabetes than in the general population (Hoepelman, Meiland, & Geerlings, 2003; Ronald & Ludwig, 2001). Additional evidence suggests that type 2 diabetes increases susceptibility to serious complications of UTI, including emphysematous conditions of the bladder or kidney, renal abscess, and renal papillary necrosis (Griffin, Bergstralhn, & Larson, 1995; Huang & Tseng, 2000; Mnif et al., 2013). Atypical and resistant forms of infection may also be more common in patients with type 2 diabetes (Stapleton, 2002). Several different mechanisms may contribute to the higher frequency of UTI and related complications among diabetic patients, including immune function impairments (Delamaire et al., 1997; Muller et al., 2005), dysfunctional bladder emptying related to autonomic neuropathy (Hosking, Bennett, & Hampton, 1978; Truzzi, Almeida, Nunes, & Sadi, 2008), and higher glucose levels in the urine which may facilitate the growth of pathogenic organisms (Chen, Jackson, & Boyko, 2009).

UTI imposes a substantial economic burden on the health system (Foxman, 2002; Foxman, Barlow, D'Arcy, Gillespie, & Sobel, 2000); nonetheless, formal evidence is limited on the direct medical cost burden of UTI specifically among diabetic patients. Given the increasing prevalence of type 2 diabetes and the clinical link between diabetic status and UTI risk and severity, there is a need to understand

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* Corresponding author. Tel.: +1 908 423 4733; fax: +1 908 735 1688.
E-mail addresses: shengsheng.yu@merck.com (S. Yu), zf54@georgetown.edu (A.Z. Fu).

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the frequency and costs associated with UTIs in patients with type 2 diabetes for resource allocation decisions in the U.S. Several large observational studies have examined the risk of UTI in diabetic populations; however, most have been restricted to female subjects due to their significantly higher risk of UTI compared to male patients (Boyko, Fihn, Scholes, Abraham, & Monsey, 2005; Boyko et al., 2002; Foxman, 2002). Other studies have measured the risk of UTI among both men and women with diabetes in settings outside of the U.S. (Al-Rubeann, Moharran, Al-Naqeb, Hassan, & Rafiullah, 2013; Hirji, Guo, Andersson, Hammar, & Gomez-Caminero, 2012; Muller et al., 2005). A recent UK-based analysis found that type 2 diabetes increased UTI incidence for both men and women, but noted variation in the relative risk across different gender and age groups (Hirji et al., 2012). The study also found additional increases in UTI risk among diabetic patients with longer duration of diabetes and among those with poor glycemic control. Given differences in patient characteristics and health care services between countries, additional population-based studies are warranted to describe in detail the age- and gender-specific prevalence of UTI among diabetic patients in the U.S.

Using a large retrospective analysis of commercial claims, we sought to examine the rate of UTI among U.S. patients diagnosed with type 2 diabetes in a managed care setting, and to estimate the additional health care resource use and costs associated with the occurrence and recurrence of UTI in the presence of type 2 diabetes.

2. Materials and methods

2.1. Data source

Data were obtained from the MarketScan Commercial Claims & Encounters and the MarketScan Medicare Supplemental and Coordination of Benefits databases covering the period from January 1, 2008 to September 9, 2011. The MarketScan databases are integrated, de-identified, patient-level data sources representing the health services of approximately 77 million individuals in all age groups since 1996, drawn from 77 employers and 12 U.S. health plans, representing over 126 unique carriers. Enrollees include individuals with primary coverage through fee-for-service or capitated health plans, including comprehensive plans, exclusive provider organizations, preferred provider organizations, point-of-service plans (with and without capitation), and health maintenance organizations. All census regions within the continental U.S. are represented in the database. Data elements capture enrollment history, demographic information, and claims for inpatient, outpatient and pharmacy services (including prescriptions from mail-order and specialty pharmacies). All MarketScan data files are compliant with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act (HIPAA).

2.2. Sample selection

A random sampling of 5 million individuals with at least one recorded diagnosis of type 2 diabetes (International Classification of Disease, 9th Revision, Clinical Modification [ICD-9 CM]: 250.xx) were drawn from the MarketScan database, and within the selected MarketScan population, those with a type 2 diabetes diagnosis between 2008 and 2009 were randomly selected and used as the starting population of the sample selection. This resulted in ~120,000 patients.

The study sample was further restricted to patients who were at least 18 years old as of the start date, defined as the first type 2 diabetes diagnosis date between 1/1/2008 and 9/30/2009, and continuously enrolled in the database for a minimum of 2 years from the start date. Patients were excluded if they had any diagnoses for type 1 diabetes mellitus (ICD-9-CM: 250.x1, 250.x3) or other forms of secondary diabetes (ICD-9-CM: 249.xx). Patients with an observed pregnancy (ICD-9-CM: 630-679, V22) during their 2-year eligibility period were also excluded from the analysis. The final study sample consisted of 73,151 patients who met the inclusion/exclusion criteria.

2.3. Study design overview

The baseline and study periods were defined respectively as the first and the second year following his/her start date. For each patient, the occurrence of UTI events was separately determined using diagnosis codes during the baseline and study period. Patients were classified into two groups based on presence of UTI events during the baseline period: prevalent cohort if he/she had a UTI event during the baseline period and incident cohort if he/she did not have any UTI event. Furthermore, among patients who had a UTI event during the study period, those who also had a UTI event during the baseline period were referred to as prevalent cases; otherwise incident cases.

The economic burden of UTI was studied in both bottom-up and top-down approaches. The bottom-up approach described UTI-related health care utilization and cost outcomes among the patients with a UTI event during the study period by measuring health care services and costs specifically associated with a UTI diagnosis code or an antibiotic prescription for UTI in prevalent versus incident cases. The top-down approach sought to comprehensively assess and compare any health care service use associated with UTIs, including potential downstream utilization and costs of UTI that may not be coded as UTI-related in the database. We estimated the total incremental burden of UTI among patients with type 2 diabetes by comparing all-cause utilization and cost outcomes in patients with versus without UTI during the study period using a matched sample. The matched sample consisted of the patients with UTIs and their 1:1 matched patients without UTIs using propensity score matching (PSM). The matched adjusted analysis aimed to estimate and compare incremental health care resource uses and cost in patients with versus without a UTI event during the study period, who otherwise had similar characteristics during the baseline period, such as: diagnosis of UTI; hypoglycemia; microvascular complications (retinopathy/blindness, neuropathy, nephropathy); cardiovascular conditions (stroke, transient ischemic attacks, congestive heart failure, myocardial infarction, ischemic heart diseases, peripheral arterial diseases); chronic kidney diseases; and liver diseases.

2.4. Variable measurement

2.4.1. Exposure and covariates

A UTI event was identified in the database using ICD-9-CM diagnosis codes, including chronic pyelonephritis (590.0), acute pyelonephritis (590.1), cystitis (595.x) and urinary tract infection, site not specified (599.0). The study focused specifically on symptomatic UTI diagnoses due to concerns that asymptomatic bacteriuria would be underdiagnosed in retrospective claims data. Patient baseline characteristics regarded as potential risk factors for UTI during the study period were included as covariates, including age, gender, residential location (rural vs. urban), census region, health plan type, Charlson Comorbidity Index (CCI), hypoglycemia, microvascular complications, cardiovascular conditions, chronic kidney diseases and liver diseases.

2.4.2. Outcome variables

Health care utilization and cost outcomes were measured. Utilization outcome variables included hospitalizations, length of stay (in days), outpatient visits and uses of antibiotics for UTI treatment. Hospital and outpatient visits were considered UTI-related if they were recorded with a UTI diagnosis code. UTI-related prescription drugs were defined as any antibiotic prescriptions filled no later than 7 days after a UTI diagnosis, or within the supply days of a previous UTI-related antibiotic drug fill. If a patient had multiple UTI-related antibiotic fills, the days of supply for each fill were combined together to compute total days of supply.

Direct health care costs were disaggregated into hospital, outpatient, and prescription drug costs. Each cost component was

calculated from a payer perspective (i.e., reimbursed amount), patient perspective (i.e., out-of-pocket spending), and combined total. There was no inflation adjustment due to the short duration of the study period.

2.5. Statistical analysis

The prevalence of UTI was calculated as the number of patients with at least 1 UTI event during the study period, divided by the total number of patients in the sample. This formula aligns with the definition of period prevalence, or the proportion of individuals who have the condition at any point during a period of time (Aschengrau & Seage, 2008). UTI prevalence was also stratified by gender and age groups.

Patient baseline characteristics were summarized for patients with versus without UTI during the study period. For continuous variables, the mean and standard deviation (SD) were reported; for binary and categorical variables, proportions were reported. Between-group differences were assessed using *t*- tests for continuous variables and chi-square tests for categorical variables. In addition, the descriptive analysis of baseline patient characteristics was conducted using the entire study sample as well as the matched sample.

In the bottom-up approach that considered UTI-related utilizations and costs, healthcare resource use was summarized by service type among those who consumed the healthcare service. Differences in resource use were assessed using *t*-tests for continuous variables and chi-square tests for binary or categorical variables. Mean and standard deviation of number of hospitalizations and total length of stay were reported among patients with at least one UTI-related hospitalization during the study period. The number of UTI-related outpatient visits was summarized among patients with a least 1 UTI-related outpatient visit during the study period. UTI-related prescription drug use was summarized among those receiving antibiotics for UTIs, in terms of the number of pharmacy claims and total number of days of supply dispensed. For each UTI-related cost component, the mean and standard deviation were summarized among the patients who incurred the cost, and UTI-related cost differences were assessed using *t*-tests.

In the top-down approach in which all-cause utilization and costs were of interest, the mean and standard deviation were reported for all patients in the matched sample. All-cause health care utilization and cost outcomes during the study period were compared between patients with and without UTIs during the study period using *t*-tests for continuous variables and chi-square tests for binary or categorical variables.

Propensity score matching was used for the comparison of all-cause health care utilization and costs between patients with and without UTI during the study period. A multivariate logistic regression model was used to estimate each subject's propensity (probability) of having a UTI diagnosis in the study period, given his/her baseline patient characteristics. Patients with UTI during the study period were one-to-one matched with patients without UTIs using a greedy-matching algorithm (Parsons, 2004). To adjust for residual differences in baseline patient characteristics between matched patients with and without UTI, a generalized linear model with log link function and gamma variance was used to compare total all-cause health care costs between the matched groups (Diehr, Yanez, Ash, Hornbrook, & Lin, 1999). Upon the fitting of the generalized linear model, the method of recycled prediction was applied to estimate the total incremental cost associated with a UTI during the study period (Basu & Rathouz, 2005).

3. Results

3.1. UTI prevalence

Of the final sample of 73,151 patients, 6,014 (8.2%) were diagnosed with a UTI during the study period. Stratified by gender, UTI was diagnosed in 4,517 (12.9%) female patients and 1,497 (3.9%) male patients. Fig. 1 further stratifies the gender-specific prevalence of UTI by age category. While the prevalence of UTI in female patients fluctuated around 12.9% across the age categories, a steady increase in the prevalence of UTI in male patients can be seen as age increases. For both male and female patients, there was a steep increase in the prevalence of UTI from the age categories of 65–74 years to 75+ years. Female patients also showed a large increase in UTI prevalence from the age groups of 18–24 years to 25–34 years.

3.2. Patient characteristics during the baseline period

The overall prevalence of UTI during the baseline period was 8.5%, similar to that observed during the study period. Two thousand thirty-two (37.2%) patients with baseline UTIs developed UTIs during the study period; 3,982 (5.95%) patients without baseline UTIs developed UTIs during the study period ($p < 0.0001$).

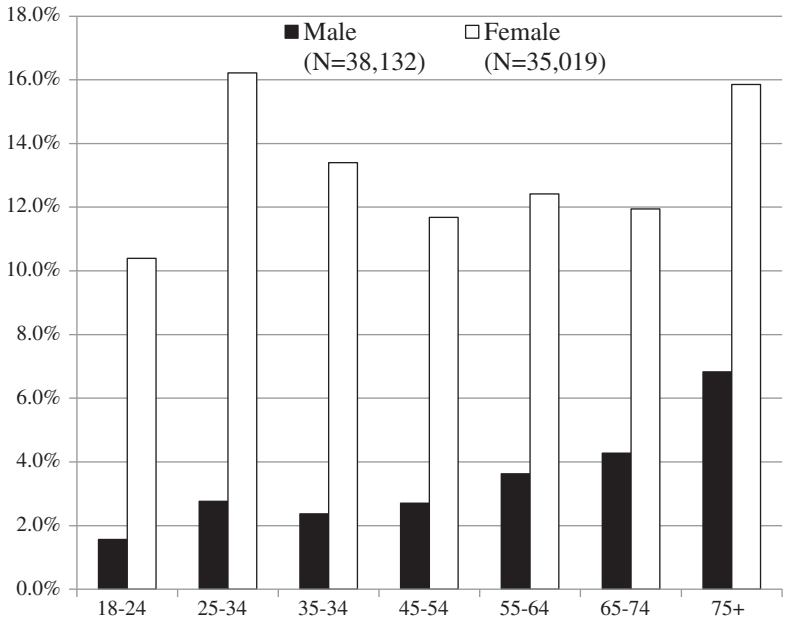
Table 1 presents the comparison of baseline characteristics between patients with and without UTI during the study period. Females comprised 75.1% of patients with UTI versus 45.4% of those without UTI ($p < 0.0001$) in the study period. Age distribution significantly differed between patients with and without UTI ($p < 0.0001$), with a larger proportion of patients with UTI during the study period falling into the age category of 25–34 year (1.6% vs. 1.3%) and 75 or older (22.5% vs. 15.8%) than controls. Overall comorbidity, measured by Charlson Comorbidity Index, also tended to be greater among those with UTI during the study period (1.024 vs. 0.710; $p < 0.0001$). Significantly more patients with UTIs during the study period also had hypoglycemia (4.2% vs. 3.1%; $p < .0001$), diabetes-related microvascular complications (22.9% vs. 18.9%; $p < .0001$), cardiovascular diseases (26.1% vs. 20.3%; $p < .0001$), chronic kidney diseases (5.9% vs. 3.9%; $p < .0001$) and liver diseases (2.7% vs. 1.9%; $p < .0001$).

After adjusting for other baseline covariates in the logistic regression for UTI propensity, ages of 75+ years (odds ratio [OR]: 1.30 vs. 55–64 years; 95% CI: 1.19, 1.42), female gender (OR: 2.96; 95% CI: 2.78, 3.15), and presence of UTI during the baseline period (OR: 5.70; 95% CI: 5.34, 6.08) continued to be the strongest predictors of UTI in the study period (results not shown).

3.3. UTI-related health care resource use and costs

Table 2 reports UTI-related utilization and cost outcomes in the prevalent versus incident cases. Approximately 10% of patients in either group had at least one UTI-related hospitalization during the study period. Among the hospitalized, mean length of stay per visit was 7.58 days (SD: 15.2) and 7.25 days (SD: 17.8) for the prevalent and incident cases, respectively ($p = 0.81$). Nearly all prevalent and incident cases had at least one UTI-related outpatient visit in the study period, but the proportion was significantly greater among prevalent cases (97.5% vs. 95.1%; $p < 0.0001$). The total number of UTI-related outpatient visits was also significantly higher in prevalent versus incident cases (2.38 vs. 1.56; $p < 0.0001$). Antibiotic treatment for UTI was more common in prevalent than incident cases (66.1% vs. 62.3%; $p = 0.003$), and antibiotic users in prevalent cases tended to have more pharmacy claims for antibiotic drugs (4.79 vs. 3.21; $p < 0.0001$) and longer days of supply (67.1 vs. 30.9; $p < 0.0001$) than those in incident cases.

On average, prevalent cases incurred significantly higher total costs of UTI-related outpatient services ($603 vs. $447; $p = 0.033$) and antibiotic prescriptions ($61 vs. $35; $p < 0.0001$) than incident cases. The cost of UTI-related inpatient services was higher in the prevalent cases than the incident cases; however, the cost differences was not statistically significantly between the two groups ($2,271 vs. $2,301; p = NS).



	18-24	25-34	35-34	45-54	55-64	65-74	75+
Male (N=38,132)	1.6%	2.8%	2.4%	2.7%	3.6%	4.3%	6.8%
Female (N=35,019)	10.4%	16.2%	13.4%	11.7%	12.4%	11.9%	15.9%

Fig. 1. Prevalence of UTI within 1-year study period, by gender and age group.

3.4. Total incremental health care resource use and costs of UTI

Six thousand and nine patients (out of 6,014) with UTI in the study period were matched to those without UTI during the study period based on the estimated propensity scores. No significant difference in baseline patient characteristics was detected after matching. Table 3 presents the matched comparison of total utilization and cost outcomes. In this matched analysis, patients with UTI had significantly more outpatient visits during the study period (24.47 vs. 17.77; $p < 0.0001$), a higher risk of hospitalization (26.73% vs. 12.66%; $p < 0.0001$), and longer duration of stays per hospitalization (1.99 vs. 0.71 days; $p < 0.0001$).

On average, patients with UTI in the study period incurred total annual hospitalization costs of $6,389 compared to $2,730 for matched patients without UTI (incremental cost: $3,659; $p < 0.0001$). Those with UTI also spent an additional $2,864 on outpatient services ($p < 0.0001$) and an additional $243 on prescription drugs ($p < 0.0001$) per patient per year, relative to those without UTI. Overall, all-cause health care spending by patients with and without UTI was, respectively, $19,562 and $12,796, for a difference of $6,766 ($p < 0.0001$).

Applying the method of recycled predictions based on the results of multivariable cost analysis, the incremental costs associated with UTI was estimated to be $7,045 (95% CI: 4,130–13,051; $p < 0.0001$) per patient with type 2 diabetes per year (results not shown).

4. Conclusions

This study examined the 1-year prevalence and health care cost implications of UTI in a large sample of adult U.S. patients diagnosed with type 2 diabetes. Overall, we observed an 8.2% risk of one or more UTI diagnoses during a year-long study period. Although female gender was a strong predictor of UTI risk, UTI was commonly diagnosed in both men (3.9%) and women (12.9%) with type 2 diabetes. The 1-year UTI prevalence of 8.2% in this study was higher than the 0.0469/patient–year incidence rate reported for UK patients with type 2 diabetes (Hirji et al., 2012), and the 7.0% prevalence reported for Dutch patients with type 2 diabetes (Muller et al., 2005). The higher frequency of UTI in our study could reflect true differences in UTI risk between diabetic patients in each country, but could also be due to differences in the comprehensiveness of the database used. The UK and Dutch studies relied on primary care medical records, which may not systematically capture UTIs diagnosed in a hospital or specialist setting.

To our knowledge, this study is the first to estimate the total direct health care cost burden of UTI specifically among patients with type 2 diabetes, a group that is predisposed to a more complicated course of UTI (Mnif et al., 2013). One recent claims database analysis reported median antibiotic treatment costs of $10 and $8, respectively, per diabetic and non-diabetic woman with at least one UTI during a 2-year period (Stellhorn, Chow, Martin, & Mehra, 2013). Yet the estimate omits the expense of UTI-related hospitalizations and outpatient visits, which we found to be larger cost drivers than antibiotics. On average, hospitalization cost was the largest UTI-related cost component among diabetic patients with UTI, even though less than 10% of these patients had a UTI-related hospitalization. Prior evidence suggests that diabetes may be a risk factor for worse outcomes in patients hospitalized with UTI (Benfield, Jensen, & Nordestgaard, 2007; de Lastours & Foxman, 2014; Kofteridis et al., 2009; Pertel & Haverstock, 2006). For example, in a case–control study of elderly patients hospitalized for acute pyelonephritis in Greece, diabetes was associated with significantly longer lengths of stay and higher risks of bacteremia complications and mortality (Kofteridis et al., 2009).

Findings from this study suggest a high cost burden of UTI among patients diagnosed with type 2 diabetes. Across all cost components, UTI-related health care cost over 1 year was approximately $2,300 per type 2 diabetes patient diagnosed with UTI, a figure that reflects observed payments for claims with a UTI diagnosis code or an antibiotic

Table 1
Baseline characteristics of type 2 diabetes patients with versus without UTI diagnosis during study period.

Baseline factors	With UTI in study period (N = 6,014)		Without UTI in study period (N = 67,137)		p-value
Age (years), mean (SD)	62.5	(13.6)	60.5	(12.4)	<0.0001
Age group (years), *n* (%)					
18–24	9	(0.2%)	132	(0.2%)	<0.0001
25–34	96	(1.6%)	856	(1.3%)	
35–44	399	(6.6%)	4,769	(7.1%)	
45–54	1,130	(18.8%)	15,007	(22.4%)	
55–64	2,211	(36.8%)	26,047	(38.8%)	
65–74	814	(13.5%)	9,712	(14.5%)	
75+	1,355	(22.5%)	10,614	(15.8%)	
Female, *n* (%)	4,517	(75.1%)	30,502	(45.4%)	<0.0001
Rural (vs. urban), *n* (%)	989	(16.5%)	11,530	(17.2%)	0.15
Residential location, *n* (%)					
Northeast	458	(7.6%)	5,819	(8.7%)	<0.0001
North central	1,688	(28.1%)	20,057	(29.9%)	
South	2,692	(44.8%)	27,885	(41.5%)	
West	1,155	(19.2%)	13,269	(19.8%)	
Unspecified	21	(0.4%)	107	(0.2%)	
Health plan type, *n* (%)					
Comprehensive	1,151	(19.6%)	11,237	(17.1%)	<0.0001
HMO	975	(16.6%)	11,717	(17.9%)	
POS	396	(6.8%)	5,622	(8.6%)	
PPO	3,157	(53.8%)	34,616	(52.7%)	
Other*	186	(3,1%)	2,438	(3.6%)	
Charlson comorbidity index, mean (SD)	1.024	(1.597)	0.710	(1.316)	<0.0001
Comorbidities, *n* (%)					
Urinary tract infections (UTIs)	2,032	(33.8%)	4,158	(6.2%)	<0.0001
Hypoglycemia	250	(4.2%)	2,050	(3.1%)	<0.0001
Microvascular complications	1,379	(22.9%)	12,718	(18.9%)	<0.0001
Retinopathy/Blindness	417	(6.9%)	4,679	(7.0%)	0.92
Neuropathy	718	(11.9%)	5,912	(8.8%)	<0.0001
Nephropathy	450	(7.5%)	3,871	(5.8%)	<0.0001
Cardiovascular conditions	1,568	(26.1%)	13,640	(20.3%)	<0.0001
Stroke	138	(2.3%)	863	(1.3%)	<0.0001
Transient ischemic attacks	139	(2.3%)	875	(1.3%)	<0.0001
Congestive heart failure	385	(6.4%)	2,608	(3.9%)	<0.0001
Myocardial infarction	123	(2.1%)	1,197	(1.8%)	0.14
Ischemic heart diseases (incl. angina)	1,007	(16.7%)	9,803	(14.6%)	<0.0001
Peripheral arterial diseases	419	(7.0%)	3,157	(4.7%)	<0.0001
Chronic kidney diseases	352	(5.9%)	2,583	(3.9%)	<0.0001
Liver diseases	164	(2.7%)	1,295	(1.9%)	<0.0001

* Other health plans include exclusive provider organizations, point of service with capitation, consumer-directed health plans, and high deductible health plans. HMO, health maintenance organization. POS, point of service. PPO, preferred provider organization.

drug code following a UTI diagnosis. Beyond UTI-related costs, the total incremental health care costs attributable to UTI were over $7,000 in the matched comparison of diabetic patients with and without UTI. Using either approach, our estimates of annual cost per type 2 diabetes patient with UTI are notably high in comparison to previous estimates of UTI's costs in the general U.S population. Foxman et al. (Foxman et al., 2000) estimated the direct medical cost burden of UTI to be $474 million in 1995 among an estimated 11.3 million women with UTI, amounting to $42 per patient with UTI per year (Foxman et al., 2000). Aside from the difference in study populations, the higher costs in our study are partly explained by inflation, health care cost growth, and potential secular trends in the management of UTI since 1995. The difference may also be driven by differences in research methods and assumptions. Of note, the 1995 estimate was derived using a micro-costing model that multiplied the expected annual number of outpatient visits and antibiotic drug fills by a unit cost; the model did not consider inpatient service costs, and assumed a maximum of one UTI event per patient per year. In contrast, the present study benefited from actual cost data recorded in study subjects' inpatient, outpatient, and prescription drug claims and may provide a more complete summary of costs that are associated with UTI.

In accordance with prior studies (de Lastours & Foxman, 2014; Ribera et al., 2006), diabetic patients with a history of UTI faced a significantly greater burden in terms of their subsequent UTI risk. We also detected differences in the annual utilization and cost burden of UTI depending on whether or not the patient had a recent history of UTI. Namely, UTI sufferers with a baseline history of UTI had more frequent UTI-related outpatient visits and antibiotic drug fills during the study period than those without a history of UTI. These findings may reflect a higher number of distinct UTI events during the year among those with a prior history of infection. It is also possible that patients with a history of UTI had more severe UTI episodes, or were more vigilant in seeking medical care when UTI symptoms occurred.

This study is subject to several limitations. Identification of UTI events was based on recorded diagnoses in claims, and would not capture any UTI events for which the patient never sought care or was able to treat with a previously-obtained antibiotic supply. Consequently, our estimates of UTI rates, utilization, and costs reflect that of UTIs diagnosed by a provider, which are probably more symptomatic and costlier than UTIs that go undiagnosed. Similarly, because type 2 diabetes was identified by diagnosis codes, study results apply specifically to patients with diagnosed type 2 diabetes and may not generalize to undiagnosed diabetic patients. Calculations of UTI-related utilization and costs rely on the accuracy and completeness of the provider's coding, and may not include all relevant costs resulting from UTI. The comparison of all-cause utilization and costs between diabetic patients with and without UTI adjusted for a variety of demographic and baseline health factors available in claims; however, the analysis may still be subject to confounding from unobserved variables, including disease duration and glycemic control. In estimating the cost burden of UTI, this study focused exclusively on direct medical expenses incurred by the insurer and the patient. A

Table 2
UTI-related health care utilization and cost among type 2 diabetes patients with UTI diagnosis during study period (n = 6,014).

UTI-related utilization and costs during 1-year study period	With baseline UTI (n = 2,032)		Without baseline UTI (n = 3,982)		p-value
Utilization					
≥1 Hospitalizations during study period, *n* (%)	194	(9.55%)	393	(9.87%)	0.69
Number of hospitalizations, mean (SD)	1.113	(0.38)	1.112	(0.60)	0.97
Length of stay per hospitalization, mean (SD)	7.58	(15.2)	7.250	(17.8)	0.81
≥1 Outpatient visits during study period, *n* (%)	1,981	(97.49%)	3,785	(95.05%)	<0.0001
Number of outpatient visits, mean (SD)	2.38	(3.06)	1.56	(1.58)	<0.0001
Use of antibiotics for UTI treatment, *n* (%)	1,343	(66.09%)	2,479	(62.26%)	0.003
Number of fills per patient–year, mean (SD)	4.8	(4.40)	3.2	(2.31)	<0.0001
Total days of supply, mean (SD)	67.1	(131.9)	30.9	(57.0)	<0.0001
Overall costs to payers and patients, mean (SD)					
Total costs	2,271	(11,318)	2,301	(13,792)	0.93
For inpatient services	1,607	(10,770)	1,819	(13,480)	0.51
For outpatient services	603	(2,874)	447	(2,271)	0.033
For pharmaceutical drugs	61	(137)	35	(115)	<0.0001
Costs to payers, mean (SD)					
Total costs	2,162	(11,251)	2,200	(13,665)	0.91
For inpatient services	1,574	(10,709)	1,778	(13,357)	0.52
For outpatient services	549	(2,848)	401	(2,240)	0.041
For pharmaceutical drugs	39	(110)	21	(103)	<0.0001
Costs to patients, mean (SD)					
Total costs	109	(263)	101	(270)	0.26
For inpatient services	32	(217)	41	(237)	0.16
For outpatient services	54	(132)	46	(123)	0.019
For pharmaceutical drugs	23	(41)	14	(24)	<0.0001

Table 3
All-cause health care utilization and cost among 1:1 matched type 2 diabetes patients with vs. without UTI diagnosis during study period.

All-cause utilization and cost during 1-year study period	With UTI in study period (N = 6,009)		Without UTI in study period (N = 6,009)		p-value
Utilization					
≥1 Hospitalizations during study period, *n* (%)	1606	(26.73%)	761	(12.66%)	<0.0001
Number of hospitalizations, mean (SD)	0.371	(0.764)	0.163	(0.500)	<0.0001
Total length of stay per patient–year, mean (SD)	1.989	(8.762)	0.710	(3.094)	<0.0001
≥1 Outpatient visits during study period, *n* (%)	6,009	(100.00%)	5,951	(99.03%)	<0.0001
Number of outpatient visits, mean (SD)	24.47	(20.47)	17.77	(17.44)	<0.0001
Use of antibiotics for UTI treatment, *n* (%)	5,838	(97.15%)	5,787	(96.31%)	0.009
Number of fills per patient–year, mean (SD)	43.4	(32.0)	37.5	(29.0)	<0.0001
Overall costs to payers and patients, mean (SD)					
Total costs	19,562	(34,948)	12,796	(26,331)	<0.0001
For inpatient services	6,389	(24,743)	2,730	(12,236)	<0.0001
For outpatient services	9,479	(17,874)	6,615	(19,350)	<0.0001
For pharmaceutical drugs	3,694	(4,606)	3,451	(4,613)	0.004
Costs to payers, mean (SD)					
Total costs	1,667	(1,472)	1,358	(2,899)	<0.0001
For inpatient services	150	(527)	84	(514)	<0.0001
For outpatient services	833	(976)	654	(2,475)	<0.0001
For pharmaceutical drugs	684	(660)	621	(589)	<0.0001
Costs to patients, mean (SD)					
Total costs	17,895	(34,434)	11,437	(25,260)	<0.0001
For inpatient services	6,239	(24,555)	2,645	(12,059)	<0.0001
For outpatient services	8,646	(17,582)	5,962	(18,473)	<0.0001
For pharmaceutical drugs	3,010	(4,237)	2,830	(4,313)	0.021

complete assessment of societal cost burden would also need to consider the indirect costs of UTI, including work loss costs due to medical visits and UTI-related disability.

In conclusion, UTI was common and caused substantially higher costs of care in a large sample of U.S. patients diagnosed with type 2 diabetes. Given the steadily increasing prevalence of type 2 diabetes, increased attention should be paid to preventing and managing UTI among patients with type 2 diabetes.

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